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February 28, 2005

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February 28, 2005
Date

Gina N. Shishima

MS Appeal Briefs
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RE: SN 08/455,683 "Methods of Identifying Agonists and Antagonists of Opioid Receptors (as Amended)" - Graeme I. Bell et al.
Our ref: ARCD:177 Client ref: UCHI:437

Commissioner:

Transmitted herewith for filing are:

1. Appeal Brief;
2. $250 check for filing the Appeal Brief; and
4. A return postcard to acknowledge receipt of these materials.

If the check is inadvertently omitted, or the amount is insufficient, or should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski L.L.P. Account No.: 50-1212/ARCD:177.

Respectfully submitted,

Gina N. Shishima
Reg. No. 45,104

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Enclosures

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Gina N. Shishima

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Bell et al.

Serial No.: 08/455,683

Filed: May 31, 1995

For: METHOD OF IDENTIFYING AGONISTS AND ANTAGONISTS

Group Art Unit: 1647

Examiner: Landsman, Robert S.

Atty. Dkt. No.: ARCD:177

APPEAL BRIEF

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APPEAL BRIEF

MS Appeal Briefs
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

Appellants hereby submit this Appeal Brief to the Board of Patent Appeals and Interferences in response to the Office Action dated September 22, 2004. The Notice of Appeal was received by the Patent Office on December 27, 2004, as indicated by the stamped postcard. The deadline for filing this brief is February 27, 2005.

The fee for filing this Appeal Brief is $250.00 and is included herewith.

It is believed that no additional fees are due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski Deposit Account No. 50-1212/ARCD:177.

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I. REAL PARTY IN INTEREST

The real parties in interest are the assignee, Arch Development Corporation, Chicago, IL, (University of Chicago) and the licensee, Adolor Corporation, Exton, Pennsylvania.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

III. STATUS OF THE CLAIMS

Claims 1-74 were filed with the original application, Serial No. 08/292,694, on August 19, 1994. This application is a divisional of the original application.

In a Preliminary Amendment filed with this application, claims 1-46 were canceled and claims 75-80 were added. In a Response under 37 C.F.R. § 1.116 to the Restriction Requirement dated October 29, 1996, Appellants elected to prosecute claims 47-52, 59, and 63-67. In a Response under 37 C.F.R. § 1.116 to the Office Action dated October 27, 1997, claims 47, 49-51, 59, and 64-65 were amended, and claims 81-90 were added. In a Response under 37 C.F.R. § 1.116 to the Office Action dated June 29, 1998, claims 47, 49, 59, and 84 were amended, and claims 91-114 were added. In a Response under 37 C.F.R. § 1.116 to the Office Action dated August 13, 1999, claims 47, 49, 59, 63, 66, 84-114 were amended.

In a Response under 37 C.F.R. § 1.116 to the Office Action dated August 10, 2000, claims 47-52, 59, 63, 65-67, and 81-90 were cancelled, claim 103 was amended, and claims 115-136 were added. In a Response under 37 C.F.R. § 1.116 to the Office Action dated January 30, 2001, claims 64, 110, and 111 were cancelled, and claims 91, 97-102, 109, 112-115, 121, 124, and 129 were amended. In a Second Submission under 37 C.F.R. § 1.129 to the Office Action dated January 30, 2001, claims 64, 110-111, 115, 124, 133, and 136 were cancelled, and claims 91, 97, 103, 109, 112, 116-118, 121, 123, and 125-129, and claims 137-143 were added.

In a Supplemental Amendment to the Office Action dated January 30, 2001, claims 103, 109,117, 129, and 137 were amended. In a Response under 37 C.F.R. § 1.116 to the Office Action dated March 12, 2002, claims 103, 109, 117, 129, and 137-140 were amended. In an Amendment under 37 C.F.R. § 1.116 filed concurrently with the appeal brief filed on March 25, 2003, claims 91-96, 103-108, 116-122, 125-132, 134, and 135 were cancelled. Claims 97-102, 109, 112-114, 123, and 137-143 were pending and placed on appeal. Subsequently, prosecution was re-opened in the Office Action Dated June 17, 2003.

In an Amendment and Response filed to the Office Action Dated June 17, 2003, claims 97, 109, 123, and 137 were amended and claims 144-156 were added. A Final Office Action Dated January 5, 2004 was superceded by an Office Action Dated January 28, 2004.

In the response to the Office Action Dated January 28, 2004, claims 97, 109, 137, and 144 were amended not in response to any rejection but to clarify the invention. A Final Office Action Dated September 22, 2004 (Evidence Appendix B, Exhibit 1) rejected claims 97-102, 109, 112-114, 123, and 137-156.

Thus, claims 1-52, 59, 63-67, 81-96, 103-108, 110, 111, 115-122, and 124-136 are canceled, and claims 53-58, 60-62, and 68-80 are withdrawn. Claims 97-102, 109, 112-114, 123, and 137-156 are currently pending, stand rejected, and are appealed (Claims Appendix, Appendix A).

IV. STATUS OF AMENDMENTS

No amendments have been filed since the Final Office Action issued.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention concerns a process for screening a substance for its ability to specifically bind to an opioid receptor, said process comprising the steps of: a) expressing a

recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11; b) contacting said substance with the recombinant opioid receptor polypeptide; and c) detecting whether said substance has an ability to specifically bind to said recombinant opioid receptor polypeptide. Specification at least on pages 12, line 30 to page 13, line 1; page 18, lines 1-23.[1]

It also covers a process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of: a) providing a recombinant opioid receptor polypeptide comprising the second extracellular loop comprising the amino acid sequence of residues 111 through 136 of SEQ ID NO:12 and encoded for by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11; b) contacting said recombinant opioid receptor polypeptide with a composition comprising said substance; c) detecting whether said substance has an ability to agonize said recombinant opioid receptor polypeptide; and d) isolating said substance if said substance has an ability to agonize the recombinant opioid receptor polypeptide. Specification at least on page 18, lines 1-23; page 21, line 19 to page 22, line 22; FIG. 1 and FIG. 4A.

In other embodiments, the present invention concerns a process of screening a substance for its ability to act as a specific agonist of a kappa opioid receptor comprising: a) expressing a chimeric recombinant opioid receptor polypeptide comprising the second extracellular loop comprising the amino acid sequence of residues 111 through 136 of SEQ ID NO:12, wherein said chimeric recombinant opioid receptor polypeptide is encoded by a nucleic acid sequence comprising 30 contiguous bases of SEQ ID NO:11; b) contacting said substance with the chimeric recombinant opioid receptor polypeptide; and c) detecting whether the substance has an

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[1] Citations to the specification identify support for the claimed invention, however, such citations in no way should be construed to constitute the only support.

ability to agonize the chimeric recombinant opioid receptor polypeptide. Specification at least on page 19, line 22 to page 20, line 26; page 21, line 19 to page 22, line 22; FIG. 1 and FIG. 4A.

The present invention includes a process of screening a substance for its ability to specifically bind to an opioid receptor, said process comprising the steps of: a) expressing a recombinant opioid receptor polypeptide comprising the second extracellular loop comprising the amino acid sequence of residues 111 through 136 of SEQ ID NO:12 and encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11; b) contacting said substance with the recombinant opioid receptor polypeptide; and c) detecting whether said substance has an ability to specifically bind to said recombinant opioid receptor polypeptide. Specification at least on page 18, lines 1-17; page 21, line 19 to page 22, line 22; FIG. 1 and FIG. 4A.

In other embodiments the invention covers a process of screening a substance for its ability to specifically bind to a recombinant polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11, said process comprising the steps of: a) expressing a recombinant polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11; b) contacting said substance with the recombinant polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11; and c) detecting whether the substance has an ability to specifically bind to said recombinant polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11. Specification at least on page 18, lines 1-17; page 21, line 19 to page 22, line 22; FIG. 1 and FIG. 4A.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 97-102, 109, 112-114, 123, and 137-143 were rejected for lack of written description under 35 U.S.C. §112, first paragraph.

VII. ARGUMENT

A. Substantial Evidence Required To Uphold Examiner's Position

As an initial matter, Appellant notes that findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706(A), (E), 1994. *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999). Moreover, the Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by "substantial evidence" within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *In re Gartside*, the Federal Circuit stated that "the 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Id.* at 1312. Accordingly, it necessarily follows that an Examiner's position on Appeal must be supported by "substantial evidence" within the record in order to be upheld by the Board of Patent Appeals and Interferences.

B. The Specification Fulfills the Written Description Requirement for the Claimed Invention

The Action rejects claims 97-102, 109, 112-114, 123, and 137-156 under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description. The Action relies upon the statement in the Office Action dated January 28, 2004 ("January 2004 Action") (Evidence Appendix B, Exhibit 2). In the January 2004 Action, it was argued that written description was lacking because the claimed method recites using a polypeptide encoded by a nucleic acid comprising at least 30, 40, 50, 75, 100 or all contiguous bases of SEQ ID NO:11 yet "SEQ ID NO:11 encodes a partial receptor sequence and nowhere in the specification do Applicants

disclose that they were in possession of the sequence of the entire opioid receptor encoded by a polynucleotide greater than SEQ ID NO:11." January 2004 Action at page 3. In the current Action (Evidence Appendix B, Exhibit 1), it is further argued that even though there may not be any legal precedent or other principle of patent law that an applicant provide one specific species—the full-length sequence—to satisfy the written description requirement, when the claims do not recite that specific species, there is a requirement that Applicant disclose a representative number of species. The Action alleges the Appellants have not done this, and it concludes, "Therefore, what is actually claimed are methods requiring an entire genus of receptors which are not adequately described." Appellants respectfully traverse this rejection.

"The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not; the applicant for a patent is therefore required 'to recount his invention in such detail that his future claims can be determined to be encompassed within his original creation.'" *Moba v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319 (Fed. Cir. 2003) (citing *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003)). An accepted standard for the written description requirement is: "Although the applicant does not have to describe exactly the subject matter claimed, the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented **what is claimed**." *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562-1563 (Fed. Cir. 1991) (emphasis added). Written description is met if "the disclosure of the application relied upon reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Lampi*, 228 F.3d at 1378. Again, Applicants emphasize that for purposes of the written description inquiry, the invention is whatever is **actually claimed**. *Vas-Cath*, 935 F.2d at 1563-1564. An inventor is "in possession" of an invention if the patent uses "such descriptive means

as words, structures, figures, diagrams, formulas, *etc.*, that fully set forth the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). As discussed in earlier responses, by providing the sequence of SEQ ID NO:11 and the encoded polypeptide (SEQ ID NO:12), Appellants were in possession of SEQ ID NO:11, which is precisely what the claims recite. The Examiner has conceded this much, though he argues that Appellants "would be entitled to claims in which the receptor ***consists*** of SEQ ID NO:11 or 12." Action at page 3.

The Examiner admits he is "not questioning the fact that **thousands** of species of polynucleotide or encoded polypeptide would fall under SEQ ID NO:11 or 12. . . ." Action at page 2-3 (emphasis added). Instead he argues that Appellants have not disclosed a **representative** number of species without further explanation. Therefore, the Examiner has not fulfilled his burden. Moreover, the Examiner's position in this case is legally and factually without merit.

1. **Burden on the Examiner Has Not Been Fulfilled**

An application must be presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. MPEP 2163.04 (citing *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)). "The examiner must, therefore, have a reasonable basis to challenge the inadequacy of the written description. The examiner has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." *Id.* (citing *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976).

The examiner has not fulfilled this burden. There is no evidence or basis for challenging the description of the present invention except to baldly assert that an adequate number of

species has not been described. All the Examiner has done is to cite a proposition of law regarding an adequate number of species without any explanation of how that proposition applies to the instant case. In fact, the examiner acknowledges the disclosure of thousands of species, but he does not provide any explanation of why this is inadequate nor does he provide any information about what a "representative number" would be.

In addition, it is not clear that the claimed invention should be scrutinized as a genus/species type of claim. The only explanation is that the methods encompass "an entire genus of receptors." Action at page 3. It appears that the sole basis for arguing the claims can be characterized as genus/species claims is that the claims recite "comprising" in the context of the "recombinant opioid receptor polypeptide" used in the processes of the invention (*e.g.*, claim 97 recites "expressing a **recombinant opioid receptor polypeptide** encoded by a nucleic acid sequence **comprising** at least 30 contiguous bases of SEQ ID NO:11"). However, this scenario is distinguishable from cases like *Regents of the Univ. of Calif. B. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997) because the claims require a specific structure (all or part of SEQ ID NO:11 and/or SEQ ID NO:12) and are not characterized in terms of function only. Consequently, the Examiner has also not set forth *why* Appellants need to provide a reasonable number of representative species in the context of the claimed invention. There can be no dispute that Appellants have described any embodiment of the claimed invention pertaining to, for example, "a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11" (claim 97) by providing SEQ ID NO:11.

Moreover, all of the claims have been rejected for this one reason even though they are of different scope, and no distinction has been made between them on this basis.

Therefore, given that it is undisputed that thousands of species are disclosed, the examiner has failed to show by a preponderance of evidence that the skilled person would not recognize that Appellants were in possession of the claimed invention. This is insufficient to meet his burden. On this basis alone the rejection is improper and should be withdrawn.

2. **A Representative Number of Species Is Described**

The MPEP sets forth the legal basis for providing an adequate number of species to satisfy the written description requirement:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

MPEP §2163.05. The claimed invention covers processes involving an opioid receptor polypeptide having or encoded by a particular sequence (either SEQ ID NO:12 and/or SEQ ID NO:11). Thus, Appellants have described a representative number of species that are representative of the entire genus because the variations of any opioid receptor polypeptide are limited by the recited structural limitations. Moreover, because of the structural recitation in the claims, a sufficient number has been disclosed because a "person of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by members of the genus in view of the species disclosed." *See* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description" Requirement, FEDERAL REGISTER, Vol. 66, No. 4 1099, 1106 (January 4, 2001).

Furthermore, the number of disclosed species is adequate because there is no evidence that there is unpredictability with respect to the remaining species. Appellants note that the

Examiner has stated on the record that "even in the absence of the full-length receptor, the artisan would know how to make and use the present invention." Action at page 3. He has also acknowledged the "wealth of knowledge of the opioid receptor art regarding how to screen for ligands of opioid receptors." *Id.* Unlike cases in which "the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed," *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004), the Examiner has not disputed that a skilled person would be able to operate the invention based on the disclosed sequences.

Appellants note that the present specification is rife with disclosure and data regarding opioid receptors. Substantial information pertaining to processes for screening a substance for its ability to specifically bind an opioid receptor can be found throughout the Specification. The entire polynucleotide sequence of SEQ ID NO:11 is found in the Specification. Examples 1-8 provide substantial information pertaining to opioid receptors and opioid receptor polypeptides, opioid receptor isolation, and opioid receptor binding studies. Specification, page 121, line 17 through page 154, line 28. Example 10 provides information pertaining to the binding domains of the kappa opioid receptor, and assays for binding to the receptor. Specification, page 165, line 26 through page 171, line 26. Additional information can be found, for example, in the background section of the Specification as well. This section provides substantial information pertaining to the structure and function of opioid receptors. Specification, page 3, line 20 through page 11, line 8. The major classes of opioid receptors are discussed, including properties of these different classes. Specification, page 3, line 20 through page 5, line 15. Binding properties and structural characteristics of opioid receptors are also discussed. Specification, page 5, line 17 through page 11, line 8. Moreover, the Examiner has already

admitted that approximately 300 known residues of the protein encoded by SEQ ID NO:11 are 95% identical to the homologous portion of the fully characterized mouse kappa opioid receptor encoded by SEQ ID NO:1 in the Office Action Dated June 17, 2003 (Evidence Appendix B, Exhibit 3). Therefore, there is no issue regarding the operability of the claimed invention in the context of written description.

Though not specifically stating this in the most recent Office Action, it appears that the only species the Examiner contends is not described is the full-length sequence. In the previous Office Action and throughout the extensive prosecution of this case, the Examiner has maintained the written description rejection on the basis that Appellants "are not entitled to claims reading on the full length opioid receptor when they were not in possession of it at the time of the present invention." Office Action Dated January 28, 2004 (Evidence Appendix B, Exhibit 2) at page 3.

Appellants again cite to *Eli Lilly*, which states "a specification may, within the meaning of §112 P1, contain a written description of a broadly claimed invention without describing all species that claim encompasses." *See also In re Vaeck*, 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991) ("It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art.") (citing *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q 214, 218 (C.C.P.A. 1976)). As argued earlier, the Examiner has not cited any legal precedent or caselaw holding that a full-length sequence is required in order to satisfy the written description requirement. Furthermore, there is simply no legal precedent or other principle of patent law that an applicant provide one specific species in order to satisfy the written description requirement when the claims do **not** recite that specific species. Disclosure of the entire sequence of a full-length opioid receptor is not required. In order for the Specification

to fully support the claimed process, the Specification must fully disclose SEQ ID NO:11, which it does. Thus, the Specification fully supports the claimed process, which pertains to SEQ ID NO:11.

In addition to failing to meet his initial burden, the Examiner's rejection of the claims for the specification's failure to disclose an adequate number of species is legally and factually unsupported. Accordingly, Appellants respectfully request reconsideration and withdrawal of the rejection.

VIII. CONCLUSION

For the above-argued reasons, Appellants respectfully request that the rejection of claims 93, 95-115, 120-134, 173 and 174 be reversed. Appellants have provided arguments that overcome the pending rejections. Appellants respectfully submit that the Examiner's conclusion that the claims should be rejected is legally and factually unsupported. It is therefore again requested that the Board overturn the Examiner's rejection.

Please date stamp and return the enclosed postcard to evidence receipt of this document.

Respectfully submitted,

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Date: February 28, 2005

APPENDIX A

CLAIMS APPENDIX

1-52. (canceled)

53. (withdrawn) The process according to claim 47, wherein said opioid receptor polypeptide is a truncated opioid receptor polypeptide.

54. (withdrawn) The process of claim 53, wherein said truncated opioid receptor polypeptide is a truncated kappa or a delta opioid receptor polypeptide.

55. (withdrawn) The process of claim 53, wherein said truncated opioid receptor polypeptide comprises amino acid residues 79 to 380 of a kappa opioid receptor polypeptide.

56. (withdrawn) The process according to claim 47, wherein said opioid receptor polypeptide is a mutant opioid receptor polypeptide.

57. (withdrawn) The process according to claim 56, wherein said mutant opioid receptor polypeptide is a mORD1 polypeptide having an asparagine at residue 95 instead of an aspartate.

58. (withdrawn) The process according to claim 47, wherein providing said opioid receptor polypeptide is transfecting a host cell with a polynucleotide that encodes an opioid receptor polypeptide to form a transformed cell and maintaining said transformed cell under biological conditions sufficient for expression of said opioid receptor polypeptide.

59. (canceled)

60. (withdrawn) The process of claim 59, wherein the opioid receptor polypeptide comprises a portion of a kappa opioid receptor polypeptide.

61. (withdrawn) The process of claim 60, wherein the opioid receptor polypeptide comprises a portion of the second extracellular loop of the kappa opioid receptor polypeptide.

62. (withdrawn) The process of claim 61, wherein the opioid receptor polypeptide comprises a negatively charged region of the second extracellular loop of the kappa opioid receptor.

63-67. (canceled)

68. (withdrawn) The process of claim 59, wherein the opioid receptor polypeptide comprises a truncated opioid receptor polypeptide.

69. (withdrawn) The process of claim 68, wherein said truncated opioid receptor polypeptide is a truncated kappa opioid receptor polypeptide.

70. (withdrawn) The process of claim 69, wherein the truncated opioid receptor polypeptide comprises amino acid residues 79 to 380 of a kappa opioid receptor polypeptide.

71. (withdrawn) The process of claim 69, wherein the truncated opioid receptor polypeptide comprises amino acid residues 167 to 228 of a kappa opioid receptor polypeptide.

72. (withdrawn) The process of claim 59, wherein the candidate specific kappa opioid receptor agonist is pre-screened determining whether the candidate has a positive charge.

73. (withdrawn) The process according to claim 59, wherein providing said opioid receptor polypeptide is transfecting a host cell with a polynucleotide that encodes an opioid receptor polypeptide to form a transformed cell and maintaining said transformed cell under biological conditions sufficient for expression of said opioid receptor polypeptide.

74. (withdrawn) A specific kappa opioid receptor agonist isolatable by the process of claim 59.

75. (withdrawn) The process according to claim 47, wherein said opioid receptor polypeptide is a delta or kappa opioid receptor polypeptide.

76. (withdrawn) The process of claim 75, wherein said polypeptide is a delta opioid receptor polypeptide.

77. (withdrawn) The process of claim 76, wherein said delta opioid receptor polypeptide comprises the amino acid residue sequence of SEQ ID NO:4.

78. (withdrawn) The process of claim 75, wherein said polypeptide is a kappa opioid receptor polypeptide.

79. (withdrawn) The process of claim 78, wherein said kappa opioid receptor polypeptide comprises the amino acid sequence of SEQ ID NO:2.

80. (withdrawn) The process of claim 78, wherein said kappa opioid receptor polypeptide comprises the amino acid sequence of SEQ ID NO:12.

81-96. (canceled)

97. (previously presented) A process of screening a substance for its ability to specifically bind to an opioid receptor, said process comprising the steps of:

a) expressing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11;

b) contacting said substance with the recombinant opioid receptor polypeptide; and

c) detecting whether said substance has an ability to specifically bind to said recombinant opioid receptor polypeptide.

98. (previously presented) The process of claim 97, wherein said opioid receptor polypeptide is encoded by a nucleic acid sequence comprising at least 40 contiguous bases of SEQ ID NO:11.

99. (previously presented) The process of claim 98, wherein said opioid receptor polypeptide is encoded by a nucleic acid sequence comprising at least 50 contiguous bases of SEQ ID NO:11.

100. (previously presented) The process of claim 99, wherein said opioid receptor polypeptide is encoded by a nucleic acid sequence comprising at least 75 contiguous bases of SEQ ID NO:11.

101. (previously presented) The process of claim 100, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 100 contiguous bases of SEQ ID NO:11.

102. (previously presented) The process of claim 101, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 680 contiguous bases of SEQ ID NO:11.

103-108. (canceled)

109. (previously presented) A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

a) providing a recombinant opioid receptor polypeptide comprising the second extracellular loop comprising the amino acid sequence of residues 111 through 136 of SEQ ID NO:12 and encoded for by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11;

b) contacting said recombinant opioid receptor polypeptide with a composition comprising said substance;

c) detecting whether said substance has an ability to agonize said recombinant opioid receptor polypeptide; and

d) isolating said substance if said substance has an ability to agonize the recombinant opioid receptor polypeptide.

110-111. (canceled)

112. (previously presented) The process of claim 109, wherein said opioid receptor polypeptide is encoded by a nucleic acid sequence comprising at least 75 contiguous bases of SEQ ID NO:11.

113. (previously presented) The process of claim 112, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 100 contiguous bases of SEQ ID NO:11.

114. (previously presented) The process of claim 113, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 680 contiguous bases of SEQ ID NO:11.

115-122. (canceled)

123. (previously presented) The process of claim 113, wherein said opioid receptor polypeptide is a kappa opioid receptor polypeptide encoded for by the polynucleotide of SEQ ID NO: 11.

124-136. (canceled)

137. (previously presented) A process of screening a substance for its ability to act as a specific agonist of a kappa opioid receptor comprising:

a) expressing a chimeric recombinant opioid receptor polypeptide comprising the second extracellular loop comprising the amino acid sequence of residues 111 through 136 of SEQ ID NO:12, wherein said chimeric recombinant opioid receptor polypeptide is encoded by a nucleic acid sequence comprising 30 contiguous bases of SEQ ID NO:11;

b) contacting said substance with the chimeric recombinant opioid receptor polypeptide; and

c) detecting whether the substance has an ability to agonize the chimeric recombinant opioid receptor polypeptide.

138. (previously presented) The process of claim 137, wherein said nucleic acid sequence comprises 40 contiguous bases of SEQ ID NO:11.

139. (previously presented) The process of claim 137, wherein said nucleic acid sequence comprises 55 contiguous bases of SEQ ID NO:11.

140. (previously presented) The process of claim 137, wherein said nucleic acid sequence comprises 70 contiguous bases of SEQ ID NO:11.

141. (previously presented) The process of claim 137, wherein a portion of the chimeric recombinant opioid receptor polypeptide comprises SEQ ID NO:14.

142. (previously presented) The process of claim 137, wherein the chimeric opioid receptor polypeptide comprises polypeptide portions of both kappa and delta opioid receptors.

143. (previously presented) The process according to claim 97 wherein the opioid receptor polypeptide is a kappa opioid receptor polypeptide comprising SEQ ID NO:12.

144. (previously amended) A process of screening a substance for its ability to specifically bind to an opioid receptor, said process comprising the steps of:

a) expressing a recombinant opioid receptor polypeptide comprising the second extracellular loop comprising the amino acid sequence of residues 111 through 136 of SEQ ID NO:12 and encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11;

b) contacting said substance with the recombinant opioid receptor polypeptide; and

c) detecting whether said substance has an ability to specifically bind to said recombinant opioid receptor polypeptide.

145. (previously presented) The process of claim 144, wherein said opioid receptor polypeptide is encoded by a nucleic acid sequence comprising at least 40 contiguous bases of SEQ ID NO:11.

146. (previously presented) The process of claim 145, wherein said opioid receptor polypeptide is encoded by a nucleic acid sequence comprising at least 50 contiguous bases of SEQ ID NO:11.

147. (previously presented) The process of claim 146, wherein said opioid receptor polypeptide is encoded by a nucleic acid sequence comprising at least 75 contiguous bases of SEQ ID NO:11.

148. (previously presented) The process of claim 147, wherein said opioid receptor polypeptide is encoded by a nucleic acid sequence comprising at least 100 contiguous bases of SEQ ID NO:11.

149. (previously presented) The process of claim 148, wherein said opioid receptor polypeptide is encoded by a nucleic acid sequence comprising at least 680 contiguous bases of SEQ ID NO:11.

150. (previously presented) The process of claim 97, wherein said substance is an antibody.

151. (previously presented) A process of screening a substance for its ability to specifically bind to a recombinant polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11, said process comprising the steps of:

a) expressing a recombinant polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11;

b) contacting said substance with the recombinant polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11; and

c) detecting whether the substance has an ability to specifically bind to said recombinant polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11.

152. (previously presented) The process of claim 151, wherein said polypeptide is encoded by a nucleic acid sequence comprising at least 40 contiguous bases of SEQ ID NO:11.

153. (previously presented) The process of claim 152, wherein said polypeptide is encoded by a nucleic acid sequence comprising at least 50 contiguous bases of SEQ ID NO:11.

154. (previously presented) The process of claim 153, wherein said polypeptide is encoded by a nucleic acid sequence comprising at least 75 contiguous bases of SEQ ID NO:11.

155. (previously presented) The process of claim 154, wherein said polypeptide is encoded by a nucleic acid sequence comprising at least 100 contiguous bases of SEQ ID NO:11.

156. (previously presented) The process of claim 155, wherein said polypeptide is encoded by a nucleic acid sequence comprising at least 680 contiguous bases of SEQ ID NO:11.

APPENDIX B

EVIDENCE APPENDIX

1. Final Office Action Dated September 22, 2004

2. Office Action Dated January 28, 2004

3. Office Action Dated June 17, 2003

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/455,683	05/31/1995	GRAEME I. BELL	ARCD:177/WIM	8952

7590 09/22/2004

DAVID L. PARKER
FULBRIGHT & JAWORSKI
600 CONGRESS AVENUE SUITE 2400
AUSTIN, TX 78701

EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

2 month due date to Provoke Advisory Action 11-22-04

Initial deadline for
Final OA - 12-22-04
Final deadline for Final OA - 03-22-05
Initial deadline for Notice of Appeal - 12-22-04

Final deadline for Notice of Appeal 03-22-05
ARCD: 177
DLP/MBW/GNS 9/22/04
dlr SD2

Office Action Summary	Application No.	Applicant(s)	
	08/455,683	BELL ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *97-102,109,112-114,123 and 137-156* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *97-102,109,112-114,123 and 137-156* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Formal Matters

A. The Amendment dated 6/30/04 has been entered into the record.

B. Claims 53-58, 60-62, 68-80, 97-102, 109, 112-114, 123, and 137-156 were pending in this application. Claims 53-58, 60-62 and 68-80 have been withdrawn as being drawn to a non-elected invention. Therefore, 97-102, 109, 112-114, 123, and 137-156 are the subject of this Office Action.

C. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 97-102, 109, 112-114, 123, and 137-156 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 2-3 of the Office Action dated 1/28/04. Applicants argue that there is no case law to support the fact that the full-length receptor must be disclosed to fulfill the written description requirement and that, for the purposes of written description, the invention is whatever is actually claimed. They argue that, by providing the sequence of SEQ ID NO:11 and the encoded polypeptide of SEQ ID NO:12, Applicants have indicated that they were in possession of SEQ ID NO:11, which is what the claims recite. They further argue that the Examiner has not disputed the thousands of species within the scope of the claims (i.e. fragments) and that "there is simply no legal precedent or other principle of patent law that an applicant provide one specific species in order to satisfy the written description requirement when the claims do not recite that specific species."

Applicants argue that the present claims are not reach-through claims since these types of claims are defined by the PTO as "claims to future inventions based on currently disclosed inventions." Applicants argue that the screening claims in the present case can be practiced with or without the full-length sequence and that there is no requirement for Applicants to disclose every conceivable and possible future embodiment. Finally, Applicants argue that using the full-length receptor in a screening assay is a future embodiment, which is not required to achieve the utility of the invention.

The Examiner's statement regarding the present claims being "reach-through" claims has been withdrawn in view of the fact that the present claims do not fit the pattern of reach-through" claims. However, the remaining arguments have been considered, but are not deemed persuasive. The Examiner is not questioning the fact that thousands of species of polynucleotide or encoded polypeptide would fall

under SEQ ID NO:11 or 12, or that Applicants have not disclosed every conceivable and possible future embodiment. The fact remains that Applicants have not disclosed a representative number of species in the genus encompassed by the claims. Therefore, whereas there may not be any legal precedent or other principle of patent law that an applicant provide one specific species in order to satisfy the written description requirement when the claims do not recite that specific species, there is a requirement that Applicants disclose a representative number of species, which they have not done. Therefore, what is actually claimed are methods requiring an entire genus of receptors which are not adequately described. Regarding Applicants' argument that they were in possession of SEQ ID NO:11, which is what the claims recite – the Examiner agrees that Applicants were in possession of SEQ ID NO:11 and that Applicants would be entitled to claims in which the receptor ***consists*** of SEQ ID NO:11 or 12. However, the claims are not limited to these exact sequences.

It is believed that all pertinent arguments have been addressed.

3. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. The rejection of claims 97-102, 109, 112-114, 123, and 137-156 under 35 USC 112, first paragraph, has been withdrawn in view of Applicants' argument that "there is no evidence or argument that a person could not make and use the claimed invention without the full-length sequence." Upon further consideration, the Examiner has concluded that, even in the absence of the full-length receptor, the artisan would know how to make and use the present invention. Even though the claims read on the full-length receptor, which Applicants have not enabled, the fact remains that the screening methods themselves would be enabled regardless of whether or not Applicants have enabled the full-length receptor itself. This is further supported by the wealth of knowledge of the opioid receptor art regarding how to screen for ligands to opioid receptors.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (571) 272-0888. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Fax draft or informal communications with the examiner should be directed to (571) 273-0888.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-0700.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
September 20, 2004

ROBERT LANDSMAN
PATENT EXAMINER

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/455,683	05/31/1995	GRAEME I. BELL	ARCD:177/WIM	8952

7590 01/28/2004

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AUSTIN, TX 78701

EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

RECEIVED
Date(s) Docketed: 4/28 of Response
& Office, 7/28/04
final deadline
FEB 04 2004
2/4/04
Client: ARCO: 177
Attorney(s): DLP/MBW/GNS
Initials: RM

10007970

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	08/455,683	BELL ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-58,60-62,68-80,97-102,109,112-114,123 and 137-156* is/are pending in the application.

4a) Of the above claim(s) *53-58,60-62 and 68-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *97-101,109,112-114,123 and 137-156* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Upon further review by the Examiner, the finality of the rejection of the last Office action has been reconsidered and, therefore, the finality of that action is withdrawn and prosecution on the merits continues.

1. Formal Matters

A. The Amendment filed 9/22/03 has been entered into the record.

B. Claims 53-58, 60-62, 68-80, 97-102, 109, 112-114, 123 and 137-143 are pending. Claims 144-156 have been added. Claims 53-58, 60-62, 68-80 have been withdrawn as being drawn to a non-elected invention. Therefore, claims 97-102, 109, 112-114, 123 and 137-156 are the subject of this Office Action.

2. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 97-102 remain rejected and claims 109, 112-114, 123 and 137-156 are also rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 2-4 of the Office Action dated 6/17/03. Applicants argue that Applicants' specification provides written description support for full-length human opioid receptors. For example, the background section of the specification provides substantial information pertaining to the structure and function of opioid receptors. specification, page 3, line 20 through page 11, line 8. The major classes of opioid receptors are discussed, including properties of these different classes. Specification, page 3, line 20 through page 5, line 15. Binding properties and structural characteristics of opioid receptors are also discussed. Applicants argue that the specification also discloses a recombinant opioid receptor encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11. Those of ordinary skill in the art understand that an opioid receptor must have certain functional characteristics. In addition, those of ordinary skill in the art would be familiar with the function of opioid receptors, which is described throughout the specification, as noted above. Thus, functional full-length opioid receptors are fully supported by the specification. required for one of skill in the art to recognize the invention. Applicants further argue that the present invention is drawn to methods of screening a substance for its ability to specifically bind to an opioid receptor by

contacting the substance with an opioid receptor polypeptide encoded by a nucleic acid sequence that has all or part of the contiguous bases of SEQ ID NO:11. Thus, the specification satisfies the written description requirement because it reasonably conveys to one of skill in the art that Applicants had possession of the claimed subject matter. In re Daniels, 144 F.3d 1452, 1456, 46 USPQ 2d 1788, 1790. The process pertains to polynucleotides that are encoded by at least 30 contiguous bases of SEQ ID NO:11. By formulating a rejection for failure to recite the entire sequence of a full-length opioid receptor and making reference to "reach through claims," the Examiner appears to suggest that knowledge of the entire sequence of a full-length opioid receptor is required to practice the claimed invention. However, this is not the case. The claims only pertain to binding of the substance to the recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11. The Examiner appears to be arguing for inadequate written description support for a limitation that is not present in the claims at issue and that "consisting of" or "comprising up to" language is not required.

These arguments have been considered, but are not deemed persuasive. Applicants general argument is that they have provided adequate written description of SEQ ID NO:11 and that the claims are drawn to SEQ ID NO:11. Therefore, Applicants deserve claims which read on methods which encompass the full length receptor comprising SEQ ID NO:11. The way the claims are worded they are, in fact, "reach through" claims. The Examiner is not questioning the fact that Applicants were in possession of SEQ ID NO:11, or fragments of SEQ ID NO:11. The issue, as also understood by Applicants is that Applicants are not in possession of the full-length protein comprising more than the bases of SEQ ID NO:11. SEQ ID NO:11 encodes a partial receptor sequence and nowhere in the specification do Applicants disclose that they were in possession of the sequence of the entire opioid receptor encoded by a polynucleotide greater than SEQ ID NO:11. Applicants have only disclosed SEQ ID NO:11 and, therefore, the claims should reflect this. Therefore, since Applicants were in possession of SEQ ID NO:11 at the time of the present invention, they would be entitled to claims which encompass up to the full length of SEQ ID NO:11. Applicants should not be entitled to claims reading on the full length opioid receptor when they were not in possession of it at the time of the present invention. One of ordinary skill in the art would not appreciate the fact that Applicants were in possession of the claimed invention, which includes the full-length opioid receptor encompassed by the currently claimed invention. It is believed that all pertinent arguments have been addressed.

3. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. Claims 97-102 remain rejected and 109, 112-114, 123 and 137-156 are also rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 2-4 of the Office Action dated 6/17/03. Applicants argue that substantial information pertaining to processes for screening a substance for its ability to specifically bind an opioid receptor can be found throughout the specification. The entire polynucleotide sequence of SEQ ID NO:11 is found in the specification. Examples 1-8 provides substantial information pertaining to opioid receptors and opioid receptor polypeptides, opioid receptor isolation, and opioid receptor binding studies and Example 10 provides information pertaining to the binding domains of the kappa receptor, and assays for binding to the receptor. Applicants argue that even though they are not required to disclose a full-length human opioid receptor to enable the claimed invention, they do so. The process, rather than requiring use of a full-length human opioid receptor polynucleotide sequence, pertains to polynucleotides that are encoded by at least 30 contiguous bases of SEQ ID NO:11. The specification fully discloses SEQ ID NO:11 and that knowledge of a full-length opioid receptor sequence is not required to practice the claimed invention. However, Applicants argue that the specification fully enables Applicants' claimed process, which pertains to SEQ ID NO:11 and not the entire sequence of a full-length opioid receptor. Disclosure of the entire sequence of a full-length opioid receptor in the specification is not required for one of skill in the art to recognize the invention. Finally, Applicants argue that no where in the claim is there a recitation of a requirement that it must be determined whether the substance is an agonist or an antagonist of the receptor. Rather, the claims only pertain to binding of the substance to the recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11. The Examiner appears to be arguing for inadequate enablement for a limitation that is not present in the claims at issue.

These arguments have been considered, but are not deemed persuasive. Applicants general argument is that they have enabled what they have claimed, which are methods comprising SEQ ID NO:11 and that the claims are drawn to SEQ ID NO:11. Therefore, Applicants deserve the breadth of these claims even though they read on methods which encompass the full length receptor comprising SEQ ID NO:11. The way the claims are worded they are, in fact, "reach through" claims. The Examiner is not questioning the fact that Applicants are not entitled to the breadth of the claims encompassing SEQ ID NO:11, or fragments of SEQ ID NO:11. The issue, as also understood by Applicants is that the claims read on the full-length protein comprising more than the bases of SEQ ID NO:11. SEQ ID NO:11 encodes a partial receptor sequence and nowhere in the specification do Applicants disclose that they have enabled the use of the entire opioid receptor encoded by a polynucleotide greater than SEQ ID

NO:11. Applicants have only disclosed SEQ ID NO:11 and, therefore, the claims should reflect this. Applicants argue that Examples 1-8 provides substantial information pertaining to opioid receptors and opioid receptor polypeptides, opioid receptor isolation, and opioid receptor binding studies and Example 10 provides information pertaining to the binding domains of the kappa receptor, and assays for binding to the receptor. However, this still does not provide enablement for the full-length protein encoded by a polynucleotide greater than SEQ ID NO:11. Therefore, since Applicants only provided guidance and working examples of methods using SEQ ID NO:11 at the time of the present invention, they would be entitled to claims which encompass up to the full length of SEQ ID NO:11. Applicants should not be entitled to claims reading on the full-length opioid receptor when they have not provided guidance and working examples of the full-length receptor at the time of the present invention. Furthermore, it would not have been predictable to one of ordinary skill in the art at the time of the present invention what the sequence is of the full-length receptor. It is believed that all pertinent arguments have been addressed.

4. Claim Rejections - 35 USC § 112, second paragraph

A. All rejections under 35 USC 112, second paragraph, have been withdraw in view of Applicants' arguments, or amendments to the claims regarding identifying agonists via a functional assay and isolating the potential agonist.

5. Conclusion

A. No claim is allowable.

Advisory information

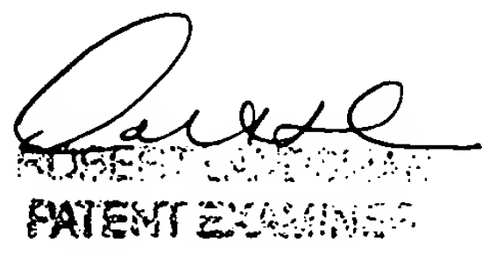
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
January 22, 2004



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/455,683	05/31/1995	GRAEME I. BELL	ARCD:177/WIM	8952

7590 06/17/2003

DAVID L. PARKER
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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/455,683	BELL ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *53-58,60-62,68-80,97-102,109,112-114,123 and 137-143* is/are pending in the application.

4a) Of the above claim(s) *53-58,60-62 and 68-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *97-102,109,112-114,123 and 137-143* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A FINAL Office Action was mailed 8/19/02 (Paper No. 40). However, upon further consideration by the Examiner, the finality of that action is withdrawn and prosecution on the merits continues.

1. Formal Matters

A. Claims 53-58, 60-62, 68-80, 97-102, 109, 112-114, 123 and 137-143 are pending. Claims 53-58, 60-62, 68-80 have been withdrawn as being drawn to a non-elected invention. Therefore, claims 97-102, 109, 112-114, 123 and 137-143 are the subject of this Office Action.

B. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 97-102 remain rejected for the reasons already of record on pages 2-3 of the Office Action dated 8/19/02. Due to the fact that the approximately 300 known residues of the protein encoded for by SEQ ID NO:11 are 95% identical to the homologous portion of the fully characterized mouse kappa opioid receptor encoded for by SEQ ID NO:1, and the fact that the second extracellular loop of each of these receptors is 100% identical, the rejection of claims 109, 112-114, 123 and 137-143 under 35 USC 112, first paragraph, has been withdrawn.

Applicants argue that the claims at issue pertain to processes for screening and processes for isolating substances for their ability to interact with an opioid receptor utilizing recombinant opioid receptor polypeptides encoding at least 30 contiguous bases of SEQ ID NO:11, which is a partial genomic sequence of a human opioid receptor. Applicants argue that the Examiner has the initial burden of presenting evidence why one of skill in the art would not recognize in Applicants' disclosure a description defined in the claims and to provide reasons why the artisan would not have recognized the description of the limitation in view of Applicants' disclosure. Applicants argue that they are not required to disclose the full-length receptor in order to provide written description support for their claims. Applicants argue that the process pertains to fragments of SEQ ID NO:11 and that the full-length protein is not required to practice the claimed invention.

These arguments have been considered, but are not deemed persuasive. Claim 97, as written, recites a process for screening a substance for its ability to specifically bind to an opioid receptor wherein the receptor comprises at least 30 contiguous bases of SEQ ID NO:11. However, claim 97 does not recite that the opioid receptor polypeptide must comprise any of the known regions (e.g. second extracellular loop) required for binding. Applicants previously argued in the Response filed 6/5/00 that the claims do not require "ligand binding" and that the claims are directed to "processes for screening a substance for its ability to interact with an opioid receptor." Applicants also argued that the Sequence Listing contains SEQ ID NO:11 and, therefore, shows "which groups of 30 nucleotides o[f] SEQ ID NO:11 will translate into a functional opioid polypeptide that can bind ligands. Though the Sequence Listing does give the nucleotide and translated amino acid sequences, the Listing does not allow one to determine which groups of 30 nucleotides are able to bind the genus of compounds which are encompassed by these claims. Applicants have only provided adequate written description of regions such as the second extracellular loop and the claims read on screening for agonists and antagonists. Without further describing in the claims the regions required for the binding of compounds other than ligands, or without limiting the claims to recite a method of screening for antibodies only, this rejection is maintained.

Applicants argument in the Appeal Brief, filed 3/28/03, that "any claim to a polypeptide comprising a particular newly discovered amino acid sequence wherein the amino acid sequence is fully disclosed in the specification could never be claimed since it is possible that the amino acid sequence might at some later point in time be attached to an object that is not presently disclosed in the specification" is incorrect. Numerous proteins are known to form dimers and it is well-known that fusion proteins can be produced using proteins, or the encoding polynucleotides. These "attachments" to the molecules of the specification would have written description if disclosed in the specification. The issue is not that all "attachments" have to be described. Applicants are implying that attaching items to a protein, such as making fusion proteins, for example, is analogous to adding polynucleotides or amino acids to a molecule to make it full-length. The issue here is not that items can't be attached to the polynucleotide of the present invention, but that the basic molecule for which attachment is necessary, is the full-length protein. Without having a start and stop codon, this polynucleotide, for example, would read on an entire gene, which is not described.

In fact, "vertebrate insulin cDNA," as argued by Applicants, is similar to "kappa opioid receptors encoded by SEQ ID NO:11" since these are, in a matter of speaking, generic statements. Neither of these terms has been adequately described to allow the artisan to identify the molecules of these genii. An artisan could no more describe any full-length proteins comprising SEQ ID NO:11 than he could describe

a full-length vertebrate insulin cDNA. In fact, unlike the kappa opioid receptor comprising SEQ ID NO:11, the structure of numerous vertebrate insulin cDNAs are well-known in the art. Therefore, in some respects, insulin cDNAs are more adequately described than are kappa opioid receptors comprising SEQ ID NO:11, since only a fragment of this receptor is described. While it is true that Applicants do not need to describe every embodiment on which the claim reads, they do need to describe the full-length receptor since these claims are currently "reach through" claims. Applicants are attempting to receive patent protection on the full-length kappa opioid receptor even though they are not in possession of this receptor. In fact, without being in possession of the full-length receptor, it is not known how Applicants can accurately determine that a compound is an agonist, or an antagonist of the receptor, as the present invention claims. It is believed that all pertinent arguments have been addressed.

3. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. Claims 97-102 are rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for a process of screening for antibodies, does not reasonably provide enablement for a process of screening for agonists, antagonists, or any other compounds which are known to require specific regions of the human kappa opioid receptor for binding or activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to Applicants claiming a screening method using any and all portions of SEQ ID NO:11 which comprise at least 30 contiguous bases of SEQ ID NO:11. Applicants have only provided guidance and working examples of proteins of SEQ ID NO:2, which is 95% identical to SEQ ID NO:12 over the 300 known residues of SEQ ID NO:12, wherein the protein comprises the second extracellular loop of SEQ ID NO:12 (which is 100% identical to that of SEQ ID NO:2). The scope of the claims reads on compounds other than antibodies. However, claim 97 does not require that the protein comprise any known amino acid regions required for the binding and/or function of ligands other than antibodies. Therefore, without the recitation of the second extracellular

loop, or other known regions disclosed as being required for binding of compounds other than antibodies, Applicants are only enabled for the screening method of claim 97 which is only used to screen antibodies. Without guidance or working examples of what residues are required in this claimed method, it is not predictable to the artisan as to what residues would be required to practice the invention of claim 97. The recitation of "at least 30 contiguous bases" is not sufficient guidance to allow the artisan to practice the invention as claimed.

In summary, the breadth of the claims is excessive with regard to Applicants claiming a screening method for any compounds other than antibodies. There is no guidance or working examples of screening methods which do not use the second extracellular loop of the protein, nor would it be predictable to the artisan which residues would be required to permit the binding of ligands other than antibodies to the receptor. For these reasons, the Examiner holds that undue experimentation is required to practice the invention as claimed.

4. Claim Rejections - 35 USC § 112, second paragraph

Claims 109, 112-114, 123 and 137-143 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 109 and 112-114 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: method steps for isolating the claimed substance. As written, it is not clear how to substance is to be isolated.

B. Claims 109, 112-114, 123 and 137-143 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a method step(s) for determining that the isolated substance is an agonist. No functional tests have been recited in the methods. Applicants are claiming a method of identifying a substance as an agonists simply by identifying its ability to bind a receptor. Binding is not necessarily indicative of functional ability.

5. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
June 16, 2003

ROBERT LANDSMAN
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